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# Effects and Limitations of Intra-aortic Balloon Pumping: An Experimental Study with Quantitated Heart Failure Model

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## I. Introduction

With the rapid progress of cardiac surgery, there has been considerable improvements in the operation results. Patients cannot be saved, however, from peri-operative and post-operative cardiogenic shock or critical heart failure derived from power failure solely by medication<sup>30,43,48,56</sup>, especially when they are old or their condition is grave. Some kind of mechanical assistance would be necessary.

Although a number of circulatory assist devices have been designed and some of them applied clinically<sup>2,6,8,16,18,19,21,22,26,32,33,36,44,51</sup>, the evaluation with respect to the indications, effects, and limitations of these devices has not been established. The absence of consensus is chiefly caused from the inconsistency in the selection of experimental methods and subjects, namely from the lack of a standard model of quantitated acute heart failure.

In the present study, the author attempted to evaluate the effects of intra-aortic balloon pumping (IABP), a technique most widely used clinically, on hemodynamic state and cardiac function, preparing a quantitated acute heart failure model by the direct injury method. The author also discussed the limitations of IABP and considered the indications of clinical application of other mechanical assist devices.

## II. Method

### 1. Animals and Operative Procedure

Forty six mongrel dogs ranging in weight from 11 to 33 kg were anesthetized with 25mg/kg of sodium pentobarbital intravenously. Anesthesia was maintained during the experiments with additional 10 mg/kg of sodium pentobarbital and 0.1 mg/kg of pancuronium bromide. Breathing of room air was controlled with a Harvard respirator through an endotracheal tube.

The left femoral artery, right femoral vein, right subclavian artery, and right carotid artery were exposed. The heart was exposed by thoracotomy at the fifth left rib and pericardiotomy.

Key Words: Cardiogenic shock, Assisted circulation, Intra-aortic balloon pumping, Experimental animal model.

索引語: 心原性ショック, 補助循環, 大動脈内バルーンパンピング, 実験モデル.

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Experimental models of acute left heart failure were then produced following the methods described by MATSUMURA<sup>28)</sup> et al.: by injecting 5N-NaOH into the myocardium at the apex of the left ventricle using injectors with 5 mm needles. Absence of backflow blood was confirmed upon injection to ensure against intravascular spillover. Locations of injection were U-stay-sutured using a Prolene® 3-0 suture with Teflon felt for hemostasis and prevention of leakage of 5N-NaOH. Although supra-ventricular and ventricular arrhythmia appeared upon injection, the influence of injection was subdued and normal sinus rhythm was restored 20 to 30 min. after the injection by moderating the injection speed, as reported by MATSUMURA et al.

The volume of injections was 0.2 ml, 0.3 ml, or 0.4 ml per kilogram of body weight, and no more than 2 ml at one site. The number of injections was limited to four times, and the injection site was moved from the apex to the base (Fig. 1).

IABP equipment (Datascope system 80) was driven carbon dioxide gas, and 10 ml-, 15 ml-, and 23 ml- single segment balloon catheters were used for intra-aortic balloon pumping according to the size of the dog. The catheter was advanced into the thoracic descending aorta via the left femoral artery. Pumping was triggered by the R wave in lead II of the electrocardiogram. The start of the inflation of the balloon was timed at the dicrotic notch in the ascending aortic pressure wave to maximize aortic diastolic pressure, and the start of deflation was timed to minimize aortic systolic pressure. Pumping rate was reduced to 1/2 of the heart rate for the dogs with high heart rates.

## 2. Classification of Experimental Groups

Twenty seven of the initial 46 dogs were studied, eliminating 15 which died of heart failure immediately after producing infarction and 4 which died because of the malfunction of a respirator.

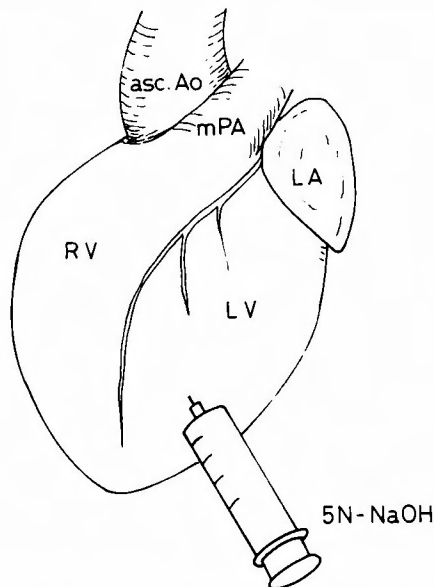


Fig. 1. Injection of 5N-NaOH into the left ventricular myocardium.

**Table 1.** Classification of experimental groups.

Group	Dosis of 5N-NaOH	I A B P	Number of dogs
1	0.2 ml/kg	-	4
2	0.2 ml/kg	+	5
3	0.3 ml/kg	-	4
4	0.3 ml/kg	+	5
5	0.4 ml/kg	-	4
6	0.4 ml/kg	+	5

These 27 dogs were classified into 6 groups according to the volume of 5N-NaOH injected and application or nonapplication of IABP (Table 1).

Hemodynamic indices before the injection of 5N-NaOH were taken as control values. For the IABP (-) group, the measurements at the point when the influence of injection procedure disappeared were adopted as immediate postinfarction values, and values were recorded every one hour thereafter until the 6th hour. For the IABP (+) group, IABP was begun with the stabilization of hemodynamic condition after the injection, and the indices were recorded every 1hr. until the 6th hr.

### 3. Methods of Measurement

- 1) Electrocardiogram was taken by limb leads. Observations were made mainly by lead II.
- 2) For ascending aortic pressure, a No. 18G Elaster needle was inserted via the right subclavian artery.
- 3) For left ventricular pressure, a No. 7F Cournand catheter was inserted via the right carotid artery.
- 4) For pulmonary arterial pressure, an Edwards No. 5F Swan-Ganz flow-directed thermodilution catheter was inserted via the right femoral vein into the main pulmonary artery.
- 5) For the right atrial pressure, an Edwards No. 5F Swan-Ganz flow-directed thermodilution catheter was inserted via the right femoral vein. In the present experiments the right atrial pressure was substituted for central venous pressure.
- 6) For left atrial pressure, a No. 18G Elaster needle was inserted through the left atrial auricle and fixed by string suture under thoracotomy.

All pressures were measured and recorded with Sanei pressure transducers (Models MPU-0.5-290 and LPU-0.1-350) and a Sanei polygraph (Model 146).

- 7) Cardiac output was determined by the thermodilution method with an Edwards cardiac output computer (Model 9520A) by injecting 5 ml of 0°C saline through a No. 5F Swan-Ganz flow-directed thermodilution catheter inserted via the right femoral vein.

### 4. Indices of Cardiac Function and Hemodynamics

- 1) For ascending aortic pressure (mmHg), systolic (sAoP), diastolic (dAoP), mean aortic (mAoP), and mean systolic aortic (msAoP) pressures were measured.
- 2) For left ventricular pressure (mmHg), systolic (SLVP), end-diastolic (LVEDP), and mean systolic (mLVSP) pressures were measured.

- 3) Left ventricular max.  $dp/dt$  (LV max  $dp/dt$ ) (mmHg/sec.) was calculated from the differential curve of the primary dimension obtained from the LV pressure curve with a Sanei differentiator (Model 1309).
- 4) For pulmonary arterial pressure (mmHg), systolic (sPAP), diastolic (dPAP), and mean pulmonary arterial (mPAP) pressures were measured.
- 5) For right atrial pressure (mmHg), mean pressure (mRAP) was measured.
- 6) For left atrial pressure (mmHg), mean pressure (mLAP) was measured.
- 7) Cardiac index (CI) (l/min./M<sup>2</sup>) and stroke volume index (SVI) (ml/M<sup>2</sup>) were calculated with the following formulas:

$$CI = \frac{\text{Cardiac Output (CO)}}{\text{Body Surface Area (BSA)}}, \quad BSA = 0.1 \times \text{body weight}^{0.725}$$

$$SVI = \frac{CI}{\text{Heart Rate (HR)}}$$

- 8) Stroke work index (SWI) (g. m/beat) and left ventricular work per minute (LVW min.) (kg.m/min.) were calculated with the following formulas:

$$SWI = SVI \times (mSLVP) \times 0.0136$$

$$LVW_{min.} = SWI \times HR \times \frac{1}{1000}$$

- 9) Total systemic vascular resistance (TSR, Hybrid Resistance Unit) was calculated by the following formula:

$$TSR = \frac{(msAoP) - mRAP}{CI}$$

- 10) Tension time index (TTI)<sup>40,41</sup> (mmHg sec/min.), diastolic pressure time index (DPTI) (mmHg sec/min.)<sup>4,40</sup>, and endocardial viability ratio (EVR)<sup>40</sup> were calculated by the following formulas:

$$TTI = msAoP \times \text{systolic time} \times HR,$$

$$DPTI = (mdAoP - LVEDP) \times \text{diastolic time} \times HR,$$

$$EVR = \frac{DPTI}{TTI}$$

Statistical probability was determined by *t*-tests and statistical significance was recognized below the 5% level.

#### 5. Measurement of Myocardial Necrosis

All the dogs were sacrificed after the experiments. Hearts were extracted, fixed with 10% solution of formaldehyde, and sliced into 5 mm-horizontal sections. The left ventricle and the necrotic areas of myocardium were weighed, and the weight ratio of the necrotic area to the left ventricle including the septum was calculated. The border areas of necrosis were stained with Hematoxylin-Eosin (H-E) and studied pathohistologically.

### III. Results

#### 1. Production of Models

2 ml of 5N-NaOH injection produced a blackish, approximately circular, swelling ranging

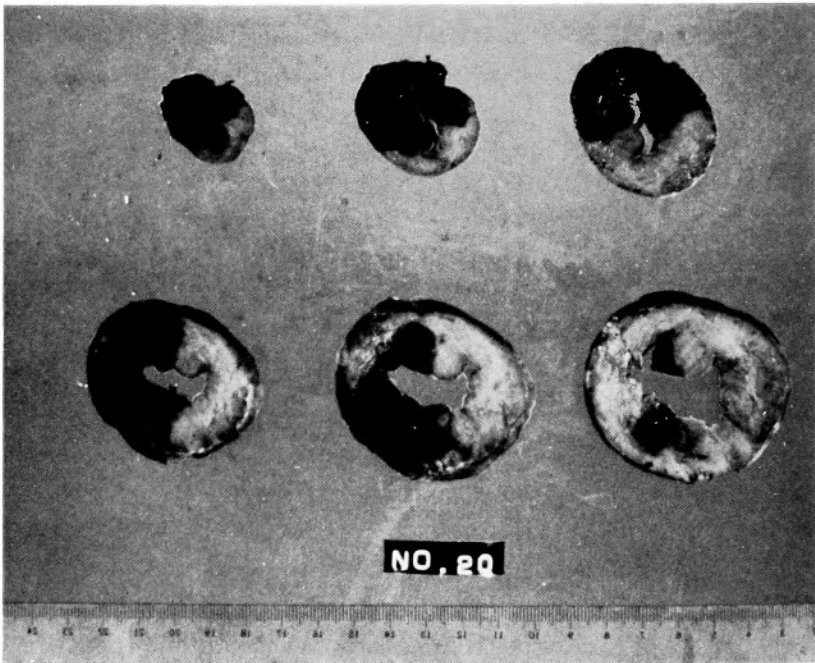
from 1.5 to 2 cm in diameter at the location of injection in all 27 dogs. It developed into a necrotic area, 2 to 3 cm in diameter, with distinct borders within 30 min. The area was apparently asynergic and was found tumor upon palpation. Cross-sectional slices macroscopically revealed that the blackish, transmural necrotic areas (Fig. 2).

Magnification ( $\times 40$ ) of the H-E stained border areas of necrosis show the normal myocardium with distinct striations, a degenerative area with indistinct striations and vacuolization of cytoplasm, and a necrotic area with karyolysis and disappearance of striations (Fig. 3). Higher magnification ( $\times 100$ ) revealed the same phenomena more clearly (Fig. 4). These pathological findings were similar to histological phenomena associated with acute myocardial infarction commonly experienced clinically<sup>15)</sup>

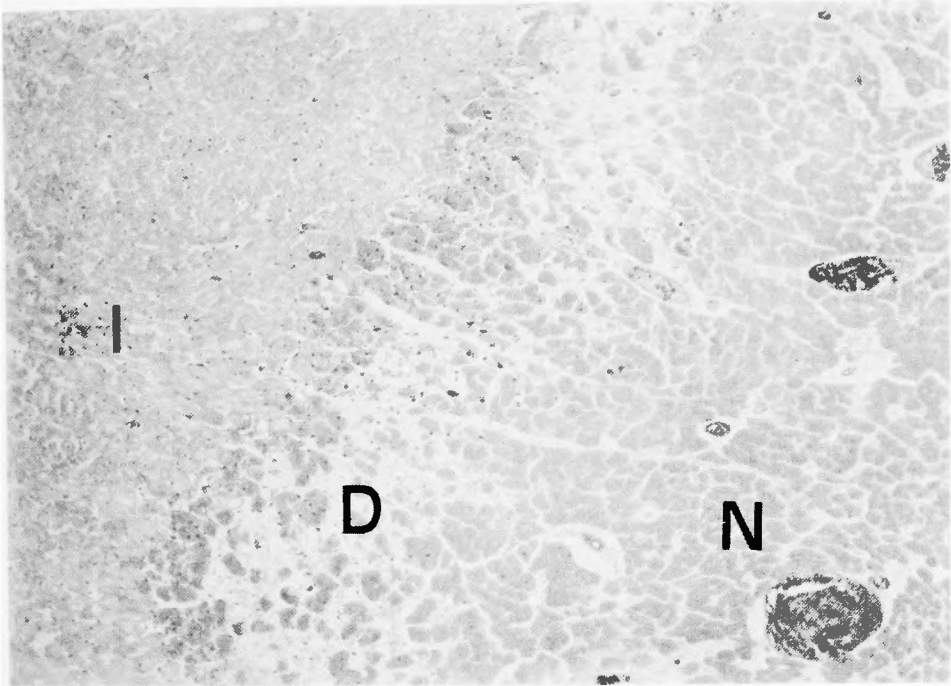
The weight ratio of the necrotic area to the left ventricle including the septum was  $19.0 \pm 4.2\%$  (mean  $\pm$  SD) for the 0.2 ml/kg-IABP (-) group,  $20.6 \pm 2.6\%$  for the 0.2 ml/kg-IABP (+) group,  $35.0 \pm 4.2\%$  for the 0.3 ml/kg-IABP (-) group,  $29.8 \pm 2.7\%$  for the 0.3 ml/kg-IABP (+) group,  $42.3 \pm 2.4\%$  for the 0.4 ml/kg-IABP (-) group, and  $37.8 \pm 2.5\%$  for the 0.4 ml/kg-IABP (+) group (Fig. 5).

The difference in the volume of injection produced significant difference in the weight of the necrotic area. The performance of IABP, however, did not produce any significant difference.

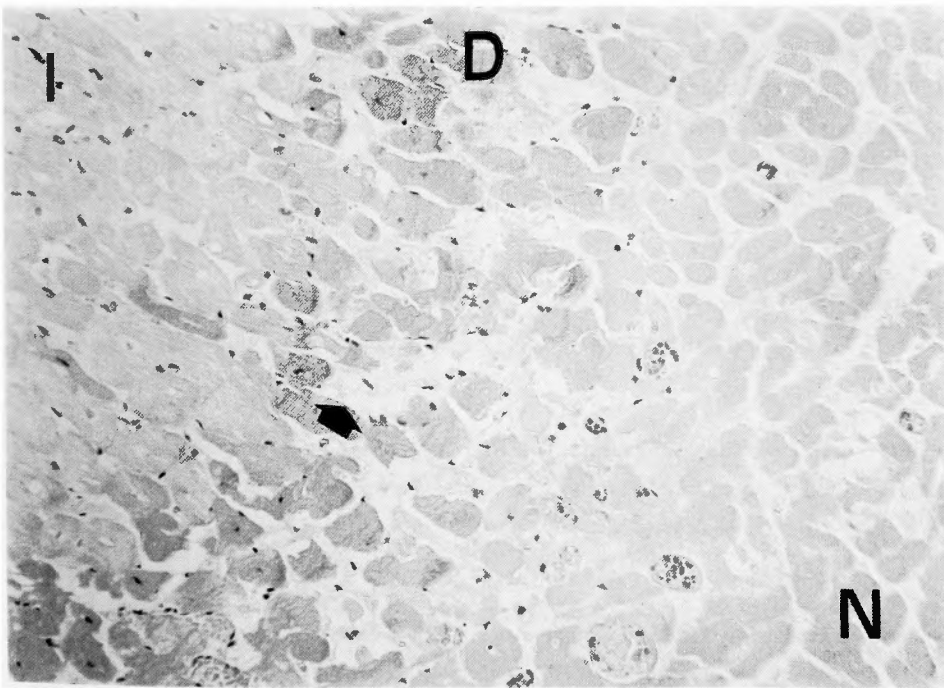
The relation between the volume of 5N-NaOH injected and the weight of the necrotic area was expressed as the regression equation,



**Fig. 2.** Transmural myocardial necrosis with distinct boundary produced by injection of 0.4 ml/Kg of 5N-NaOH (necrosis ratio-41%) extending to the anterior left ventricular wall.



**Fig. 3.** Myocardium of a dog sacrificed about 7 hr after injection of 5N-NaOH (H-E stain,  $\times 40$ ). Necrotic area (N) is sharply demarcated from normal area (I) with a narrow zone of degenerative myocardium (D).



**Fig. 4.** Necrotic myocardial fibers (N) without nuclei and striations, degenerative fibers (D) with vacuolized cells (\*), and normal fibers (I) with edematous interstitium adjacent to the degenerative area, shown in higher magnification (H-E stain,  $\times 100$ ).

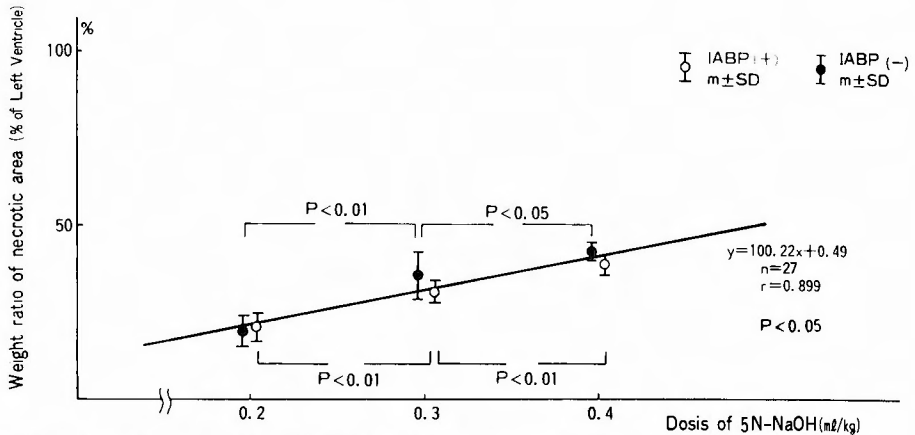


Fig. 5. Relation between 5N-NaOH injection volume and weight ratio of necrotic area.

$$y = 100.22x + 0.49 \quad (n = 27, r = 0.899, p < 0.05).$$

A strong positive correlation was observed.

Fifteen of the 46 dogs died of cardiogenic shock: 1 with 0.2 ml/kg, 6 with 0.3 ml/kg, and 8 with 0.4 ml/kg of injection. The one with the dose of 0.2 ml/kg died within 2 hr, and the others died within 1 hr.

As to the 27 models of infarction: SLVP, LVEDP, LVmax  $dp/dt$ , CI, SVI, SWI, and LVWmin. decreased significantly and the changes in other indices were insignificant for the groups with the doses of 0.2 ml/kg and 0.3 ml/kg (Table 2). Indices other than HR, mRAP, and mPAP for the groups with the dose of 0.4 ml/kg, however, dropped more sharply than for the other groups, indicating the left ventricular failure was graver in this group.

The relation between the weight of the necrotic area and the change in CI was represented as the regression equation.

$$y = -1.53x + 95.69 \quad (n = 27, r = -0.763, p < 0.05).$$

A strong negative correlation was confirmed (Fig. 6). The change in CI was expressed as the ratio of the CI value immediately after injection of 5N-NaOH to the control value.

#### Summary for the Section

It was confirmed that the volume of 5N-NaOH injection determines the weight of the necrotic area, which in turn determines the seriousness of the ventricular failure. The models of acute heart failure used in this study were successfully quantitated.

#### 2. Effect of IABP on Acute Left Ventricular Failure

In each group of injection volumes, change in indices of hemodynamic and cardiac function is shown as ratios of values immediately after injection of 5N-NaOH, 3hr, and 6hr later, setting the control values at 100.

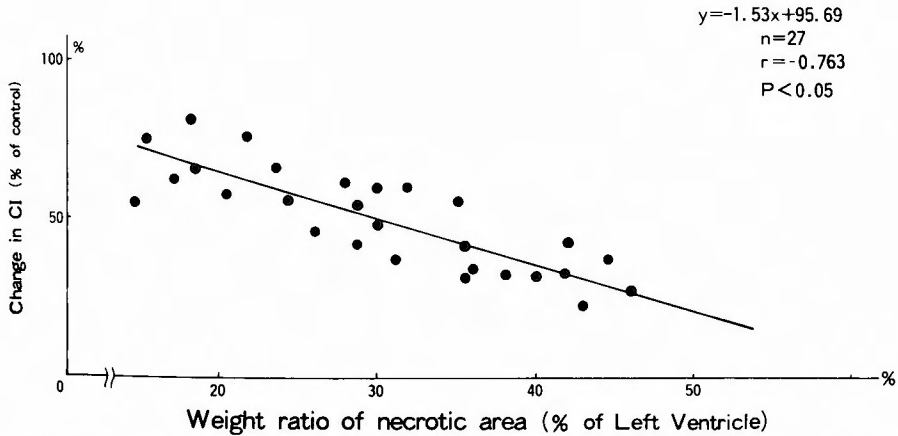
##### 1) Indices of Hemodynamics



**Table 2.** Changes in hemodynamic state immediately after 5N-NaOH injection.

Index	Group	0.2 ml/kg		0.3 ml/kg		0.4 ml/kg	
		control	post inj.	control	post inj.	control	post inj.
H R		175 ± 28.6	169 ± 21.0	163 ± 25.0	150 ± 20.3	155 ± 26.5	143 ± 25.1
sAoP		142 ± 16.4	116 ± 35.7	123 ± 34.1	88.6 ± 38.6	147 ± 27.7	70.6 ± 17.9 *
dAoP		109 ± 15.0	83.0 ± 27.0	△ 87.0 ± 27.4	59.4 ± 27.1	⊙ 103 ± 20.0	58.6 ± 19.6 *
mAoP		104 ± 29.7	95.0 ± 30.9	99.6 ± 28.4	72.4 ± 31.9	117 ± 18.7	65 ± 15.3 *
mPAP		22.6 ± 10.7	24.3 ± 10.6	19.1 ± 6.8	19.9 ± 4.6	20.7 ± 5.8	23.2 ± 3.6
mRAP		6.4 ± 3.0	6.7 ± 3.5	5.8 ± 2.3	7.8 ± 2.2	5.6 ± 2.7	8.1 ± 3.6
C I		4.00 ± 0.50	2.61 ± 1.04	⊙ 3.85 ± 1.78	1.99 ± 1.30	△ 3.81 ± 0.93	1.43 ± 0.56 *
S V I		23.5 ± 4.8	15.4 ± 6.1	▲ 24.4 ± 11.9	14.1 ± 13.6	26.3 ± 5.9	10.3 ± 4.5 *
T S R		28.8 ± 10.5	38.1 ± 11.4	27.7 ± 9.3	33.4 ± 10.2	27.9 ± 3.9	41.7 ± 15.5 ⊙
SLVP		153 ± 17.6	119 ± 39.3	△ 131 ± 36.4	94.0 ± 41.2	154 ± 25.4	73 ± 16.5 *
LVEDP		8.1 ± 4.4	13.4 ± 4.8	△ 6.9 ± 3.5	11.2 ± 4.9	△ 6.4 ± 2.0	16.6 ± 6.5 *
LVmax dp/dt		1651 ± 312	1115 ± 472	△ 1449 ± 531	925 ± 500	△ 1784 ± 355	604 ± 184 *
mLAP		8.8 ± 3.9	10.1 ± 4.0	7.3 ± 2.5	10.2 ± 3.1	△ 6.6 ± 1.9	15.9 ± 5.9 *
SW I		29.6 ± 8.0	19.6 ± 9.3	△ 24.4 ± 11.9	14.1 ± 10.0	36.1 ± 18.4	6.8 ± 3.5 †
LVWmin		5.08 ± 1.13	3.26 ± 1.71	△ 4.12 ± 2.11	2.07 ± 1.80	△ 5.35 ± 2.09	0.94 ± 0.47 *
T T I		3173 ± 362	2641 ± 802	2723 ± 908	2045 ± 861	2801 ± 575	1760 ± 517 *
DPT I		3583 ± 682	2571 ± 1088	△ 3082 ± 1127	1655 ± 905	▲ 3515 ± 913	1455 ± 711 *
E V R		1.14 ± 0.23	0.95 ± 0.30	1.13 ± 0.18	0.77 ± 0.21	⊙ 1.23 ± 0.25	0.79 ± 0.23 ⊙

(mean ± S.D.) none N.S.  
 △ P < 0.05  
 ▲ P < 0.01  
 ⊙ P < 0.005  
 † P < 0.001



**Fig. 6.** Relation between CI and Weight ratio of necrotic area immediately after 5N-NaOH injection.

Table 3. Consecutive changes in hemodynamic indices.

	0.2 ml/kg			0.3 ml/kg			0.4 ml/kg			mean $\pm$ SE upper IABP(-) lower IABP(+)
	immediately after inj.	3 hs after inj.	6 hs after inj.	immediately after inj.	3 hs. after inj.	6 hs after inj.	immediately after inj.	3 hs. after inj.	6 hs. after inj.	
H R	96 $\pm$ 6	87 $\pm$ 7	82 $\pm$ 6	85 $\pm$ 6	75 $\pm$ 7	65 $\pm$ 6	84 $\pm$ 8	66 $\pm$ 4	62 $\pm$ 9	
	94 $\pm$ 4	98 $\pm$ 6	97 $\pm$ 7	99 $\pm$ 6	94 $\pm$ 8	73 $\pm$ 9	99 $\pm$ 9	92 $\pm$ 4 <sup>⊙</sup>	86 $\pm$ 4 <sup>▲</sup>	
mAoP	72 $\pm$ 12	93 $\pm$ 7	100 $\pm$ 10	76 $\pm$ 8	113 $\pm$ 3	88 $\pm$ 7	49 $\pm$ 15	72 $\pm$ 15	93 $\pm$ 22	
	79 $\pm$ 15	119 $\pm$ 5 <sup>▲</sup>	115 $\pm$ 6	69 $\pm$ 22	118 $\pm$ 23	129 $\pm$ 12 <sup>▲</sup>	45 $\pm$ 6	87 $\pm$ 10	87 $\pm$ 16	
mPAP	100 $\pm$ 32	108 $\pm$ 53	96 $\pm$ 25	107 $\pm$ 15	107 $\pm$ 10	105 $\pm$ 9	109 $\pm$ 12	116 $\pm$ 15	137 $\pm$ 41	
	117 $\pm$ 16	131 $\pm$ 18	128 $\pm$ 19	114 $\pm$ 10	118 $\pm$ 8	121 $\pm$ 22	116 $\pm$ 10	141 $\pm$ 10	143 $\pm$ 12	
mRAP	122 $\pm$ 36	87 $\pm$ 36	122 $\pm$ 12	129 $\pm$ 29	151 $\pm$ 30	196 $\pm$ 25	139 $\pm$ 40	168 $\pm$ 44	188 $\pm$ 40	
	114 $\pm$ 17	125 $\pm$ 10	125 $\pm$ 12	118 $\pm$ 14	92 $\pm$ 25	147 $\pm$ 15	147 $\pm$ 23	182 $\pm$ 25	186 $\pm$ 25	
C I	70 $\pm$ 15	65 $\pm$ 5	56 $\pm$ 10	59 $\pm$ 16	41 $\pm$ 7	32 $\pm$ 2	40 $\pm$ 6	32 $\pm$ 6	26 $\pm$ 4	
	66 $\pm$ 12	68 $\pm$ 7	74 $\pm$ 7	47 $\pm$ 15	62 $\pm$ 18	56 $\pm$ 7 <sup>▲</sup>	36 $\pm$ 7	39 $\pm$ 7	32 $\pm$ 4	
SVI	70 $\pm$ 18	59 $\pm$ 3	64 $\pm$ 12	73 $\pm$ 27	56 $\pm$ 12	48 $\pm$ 6	39 $\pm$ 26	46 $\pm$ 7	42 $\pm$ 5	
	62 $\pm$ 12	67 $\pm$ 10	75 $\pm$ 10	68 $\pm$ 20	94 $\pm$ 25	104 $\pm$ 17 <sup>▲</sup>	38 $\pm$ 10	42 $\pm$ 8	35 $\pm$ 5	
TSR	128 $\pm$ 25	146 $\pm$ 22	178 $\pm$ 35	115 $\pm$ 20	249 $\pm$ 32	292 $\pm$ 42	159 $\pm$ 27	235 $\pm$ 31	353 $\pm$ 69	
	134 $\pm$ 15	188 $\pm$ 31	161 $\pm$ 28	126 $\pm$ 22	186 $\pm$ 34	225 $\pm$ 23	143 $\pm$ 30	207 $\pm$ 27	300 $\pm$ 55	

none NS  
▲ P < 0.01  
⊙ P < 0.005

a) HR

In all groups of different injection volumes, the IABP (-) group had a tendency to consecutive bradycardia, which became more evident with the increase in the injection volume. This tendency was weak for the IABP (+) group, and the HR of this group remained significantly higher than that of the IABP (-) group in the 0.4 ml/kg group 3 hr and 6hr after the injection ( $p < 0.005$  and  $p < 0.01$ , respectively) (Fig. 7).

b) mAoP

Mean AoP dropped immediately after the injection and consecutively increased thereafter. The decline after the injection was sharper as the injection volume increase. mAoP was higher for the IABP (+) than for the IABP (-) group, and the difference between the

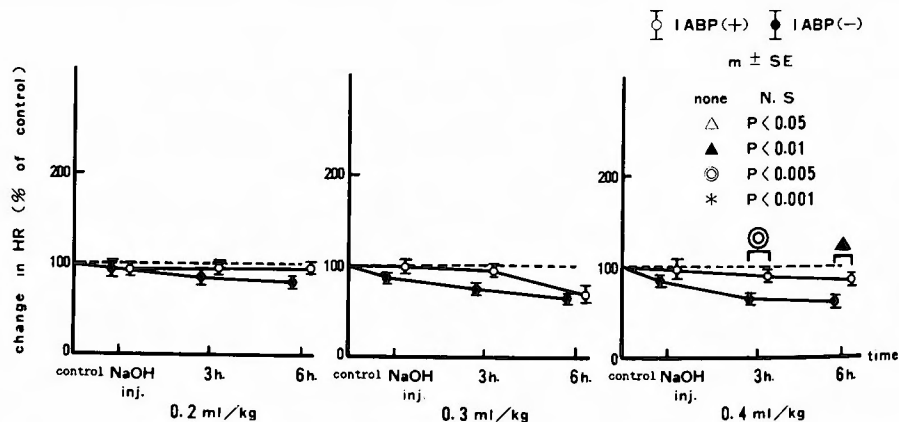


Fig. 7. Consecutive changes in HR after 5N-NaOH injection.

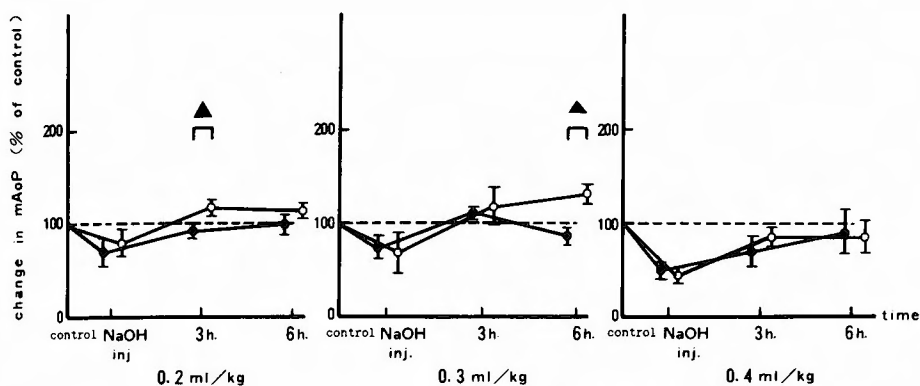


Fig. 8. Consecutive changes in mAoP after 5N-NaOH injection.

two groups was statistically significant in the 0.2 ml/kg and 0.3 ml/kg groups 3 hr and 6hr after the injection respectively ( $p < 0.01$  for both). No significant difference was observed, however, between the IABP (+) and IABP (-) groups in the 0.4 ml/kg group until the 6th hr of the experiment (Fig. 8).

c) mPAP

Mean PAP tended to increase with time. The difference between the IABP (+) and IABP (-) groups was not significant (Fig. 9).

d) mRAP

Although mRAP increased with the injection volume and time, the effect of IABP application was negligible. In the 0.3 ml/kg-injection group, the IABP (+) group tended to have lower mRAP than the IABP (-) group (Fig. 10).

e) CI

CI had a tendency to decline consecutively for the IABP (-) group, and a tendency to increase for the IABP (+) group in the 0.2 ml/kg and 0.3 ml/kg groups immediately after the injection. It was significantly higher for the IABP (+) than for the IABP (-) group

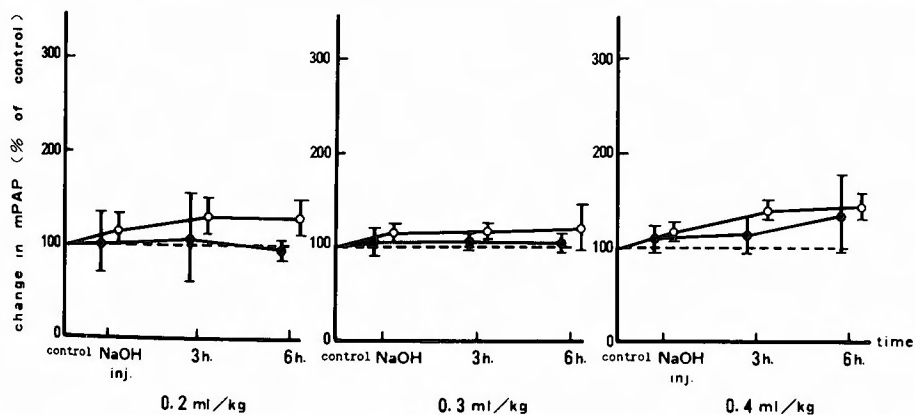


Fig. 9. Consecutive changes in mPAP after 5N-NaOH injection.

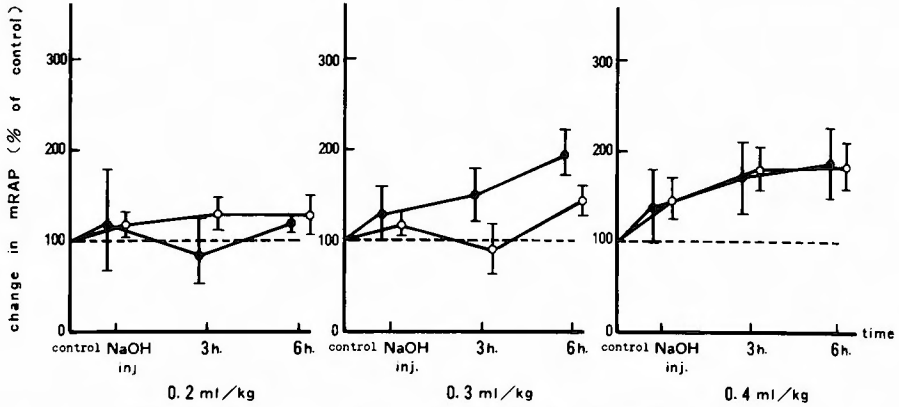


Fig. 10. Consecutive changes in mRAP after 5N-NaOH injection.

in the 0.3 ml/kg group 6hr after the injection ( $p < 0.01$ ). In the 0.4 ml/kg group, however, it declined immediately after the injection and consecutively thereafter for the IABP (+) group, and no significant difference was observed between the IABP (+) and IABP (-) groups (Fig. 11).

f) SVI

Observations were similar to those on CI: In the 0.3 ml/kg-injection group, SVI for the IABP (+) group was significantly higher than for the IABP (-) group 6hr after producing necrosis ( $p < 0.01$ ), recovering the control value in terms of the mean (Fig. 12).

g) TSR

TSR increased consecutively with the injection volume. Although there was no significant difference between the IABP (+) and IABP (-) groups, TSR for the IABP (+) group tended to be lower constantly, and the tendency was most distinct in the 0.3 ml/kg group (Fig. 13).

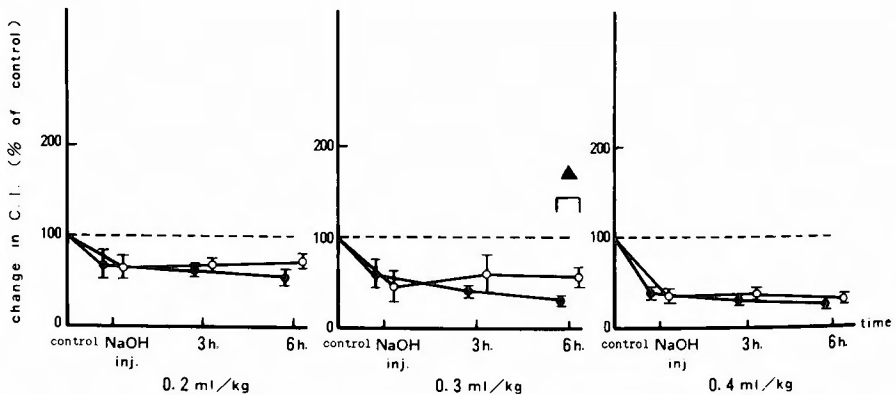


Fig. 11. Consecutive changes in CI after 5N-NaOH injection.

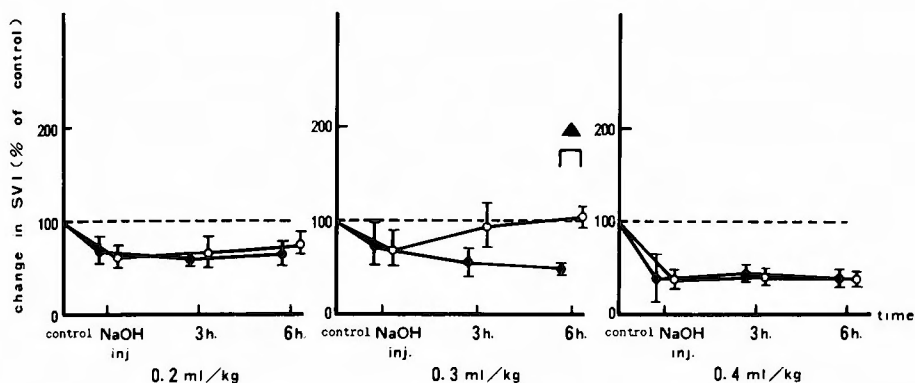


Fig. 12. Consecutive changes in SVI after 5N-NaOH injection.

#### Summary for the Section:

Performance of IABP improved the hemodynamic condition of the quantitated acute left heart failure models prepared for the present experiments: Mean aortic pressure was elevated, heart rate maintained, SVI and CI increased. Right atrial pressure, an index of the function of the right heart, was also decreased, although not significantly, and as a result, TSR tended to decrease in the IABP (+) group. This decrease was produced supposedly by the alleviation of afterload due to IABP. The effects of IABP were evident in the 0.3 ml/kg-injection group but insignificant in the 0.4 ml/kg group.

#### 2) Indices of Cardiac Function

##### a) SLVP

SLVP was not significantly different between the IABP (+) and IABP (-) groups. It recovered the control value 6hr after producing necrosis for the 0.2 ml/kg- and 0.3 ml/kg-injection groups, although it remained 75% of the control value for the 0.4 ml/kg group 6hr after injection (Fig. 14).

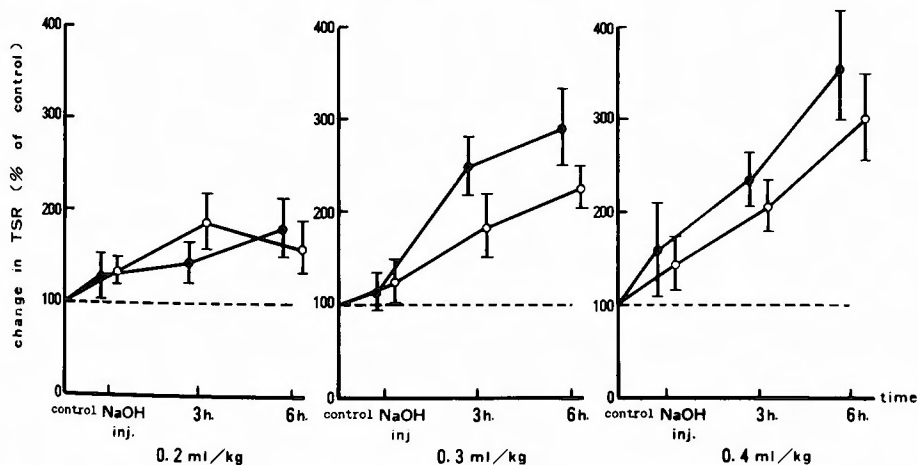


Fig. 13. Consecutive changes in TSR after 5N-NaOH injection.

Table 4. Consecutive changes in indices of cardiac function.

	0.2 ml/kg			0.3 ml/kg			0.4 ml/kg			mean ± SE upper IABP lower IABP
	immediately after inj.	3 hs. after inj.	6 hs. after inj.	immediately after inj.	3 hs. after inj.	6 hs. after inj.	immediately after inj.	3 hs. after inj.	6 hs. after inj.	
SLVP	75 ± 13 78 ± 15	93 ± 5 103 ± 4	95 ± 7 104 ± 6	71 ± 10 73 ± 21	100 ± 6 104 ± 20	98 ± 9 113 ± 18	53 ± 50 45 ± 7	65 ± 10 72 ± 9	78 ± 18 76 ± 14	
LVmax dp/dt	69 ± 15 63 ± 15	73 ± 4 84 ± 9	79 ± 5 83 ± 13	58 ± 3 69 ± 26	75 ± 13 88 ± 25	72 ± 13 85 ± 21	35 ± 7 33 ± 3	45 ± 5 59 ± 10	54 ± 11 60 ± 15	
LVEDP	163 ± 41 158 ± 20	156 ± 71 213 ± 37	211 ± 37 193 ± 16	161 ± 24 144 ± 16	185 ± 17 112 ± 36	201 ± 74 174 ± 40	190 ± 43 230 ± 43	238 ± 30 237 ± 12	264 ± 35 286 ± 10	
mLAP	128 ± 29 119 ± 9	151 ± 83 133 ± 18	145 ± 37 117 ± 7	123 ± 27 120 ± 10	141 ± 21 119 ± 18	163 ± 32 148 ± 16	181 ± 46 238 ± 24	216 ± 47 209 ± 17	258 ± 40 224 ± 12	
SWI	64 ± 22 62 ± 12	67 ± 18 67 ± 10	67 ± 18 75 ± 11	53 ± 28 46 ± 28	62 ± 19 75 ± 23	61 ± 12 131 ± 10 <sup>⊙</sup>	25 ± 4 16 ± 5	39 ± 10 29 ± 8	35 ± 5 25 ± 6	
LVWmin.	61 ± 21 40 ± 12	64 ± 17 68 ± 9	57 ± 9 78 ± 8	54 ± 17 44 ± 28	45 ± 11 74 ± 22	40 ± 6 120 ± 8 <sup>*</sup>	20 ± 5 16 ± 4	27 ± 8 49 ± 20	23 ± 7 23 ± 5	
EVR	63 ± 16 87 ± 9	116 ± 13 115 ± 18	138 ± 9 116 ± 12	74 ± 8 65 ± 9	112 ± 7 113 ± 12	114 ± 11 145 ± 3 <sup>▲</sup>	76 ± 10 65 ± 6	103 ± 9 116 ± 5	116 ± 16 128 ± 7	

none NS  
 ● P < 0.01  
 ⊙ P < 0.005  
 ▲ P < 0.001

b) LVmax dp/dt

LVmax dp/dt decreased from the control values in all groups of different 5N-NaOH doses, with the sharpest decline in the 0.4 ml/kg group. The difference between the IABP (+) and IABP (-) groups was not significant, although the IABP (+) group had a slightly higher mean value in the 0.3 ml/kg group (Fig. 15).

c) LVEDP

LVEDP was not significantly different between the IABP (+) and IABP (-) groups, although it tended to be lower for the IABP (+) group in the 0.3 ml/kg group 3hr after producing necrosis (Fig. 16).

d) mLAP

As in the case of LVEDP, mLAP was not significantly different between the IABP (+)

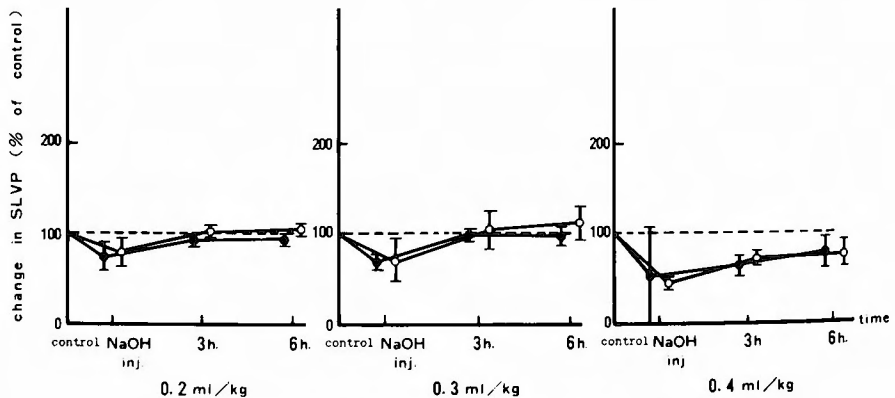


Fig. 14. Consecutive changes in SLVP after 5N-NaOH injection.

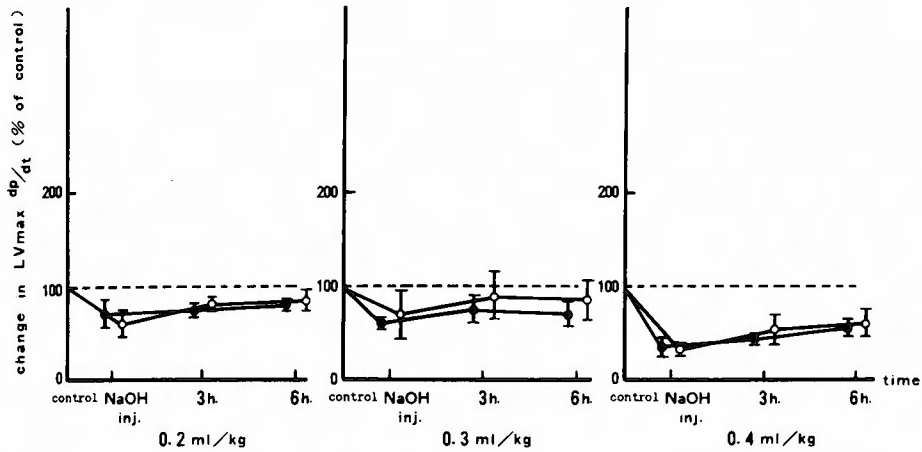


Fig. 15. Consecutive changes in LVmax.  $dp/dt$  after 5N-NaOH injection.

and IABP (-) groups, although it tended to be lower for the IABP (+) group in the 0.3 ml/kg group 3hr after producing necrosis (Fig. 17).

e) SWI

SWI for the IABP (-) group declined with the increase of the necrotic area and with time. For the IABP (+) group in the 0.2 ml/kg and 0.3 ml/kg groups, it tended to rise immediately after producing necrosis, and the difference between the IABP (+) and IABP (-) groups became significantly large in the 0.3 ml/kg group 6hr after producing necrosis ( $p < 0.005$ ). In the 0.4 ml/kg group, however, it declined with time as in the case of the IABP (-) group (Fig. 18).

f) LVWmin.

LVWmin. showed a similar pattern of change to SWI, with a significantly higher value

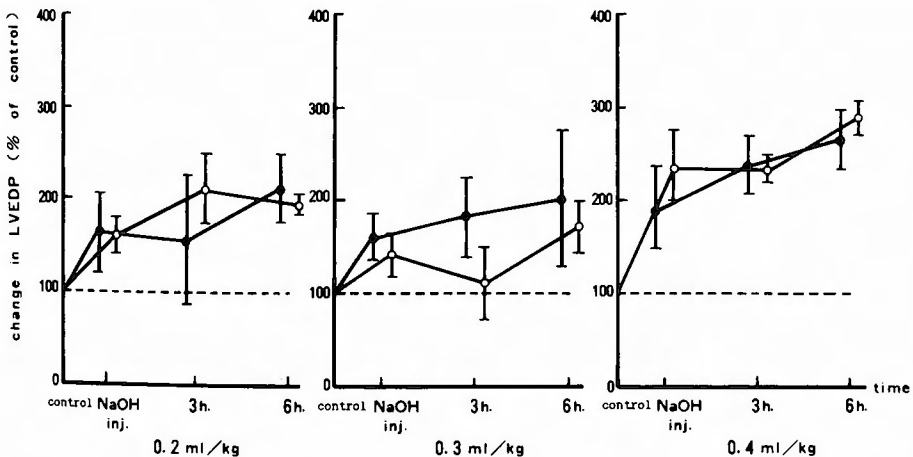


Fig. 16. Consecutive changes in LVEDP after 5N-NaOH injection.

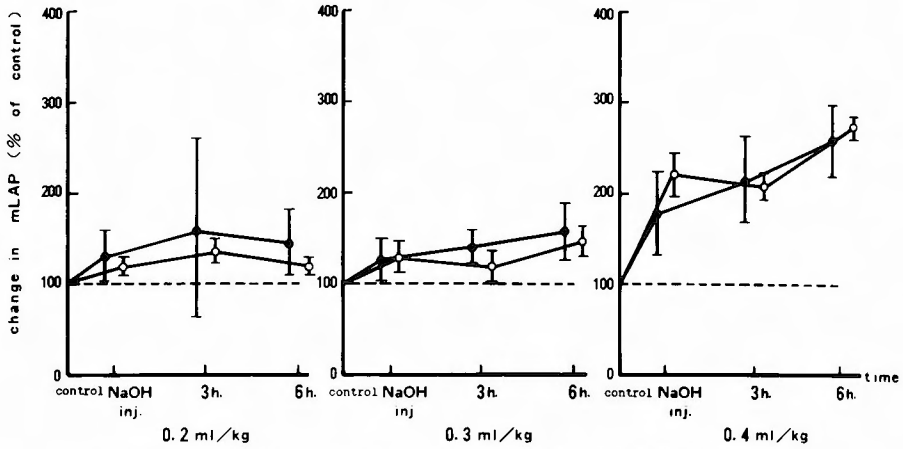


Fig. 17. Consecutive changes in m LAP after 5N-NaOH injection.

for the IABP (+) group in the 0.3 ml/kg group 6hr after producing necrosis ( $p < 0.001$ ) (Fig. 19).

g) EVR

EVR dropped immediately after producing necrosis and climbed thereafter with time. It tended to be lower for the IABP (+) group than for the IABP (-) group in the 0.2 ml/kg group but higher for the IABP (+) group in the 0.3 ml/kg and 0.4 ml/kg groups, with a significant difference between the IABP (+) and IABP (-) groups in the 0.3 ml/kg 6hr after producing necrosis ( $p < 0.01$ ) (Fig. 20).

Summary for the Section

LVEDP, an index of the compliance of the ventricle, was generally lower for the IABP (+) than for the IABP (-) group. This, along with the decrease in afterload, seems to be due to the decrease in the systolic impedance of the left ventricle brought about by IABP. LVmax  $dp/dt$ , an index of contractility, is determined by the preload, contraction force of the myocardium, and afterload. Relatively high values of LVmax.  $dp/dt$  in the present experiment may have

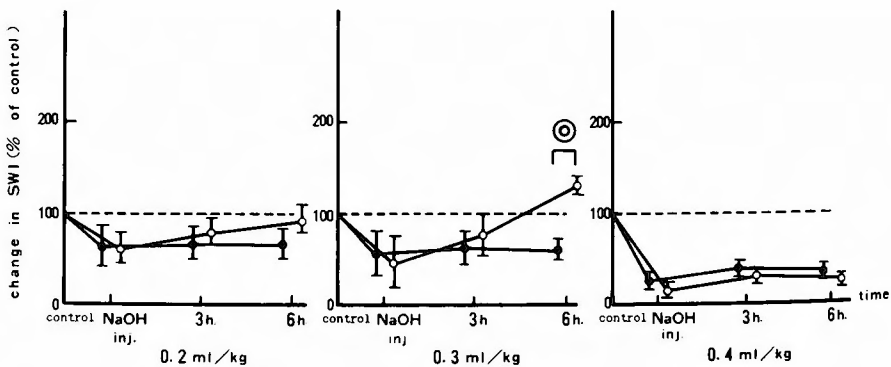


Fig. 18. Consecutive changes in SWI after 5N-NaOH injection.



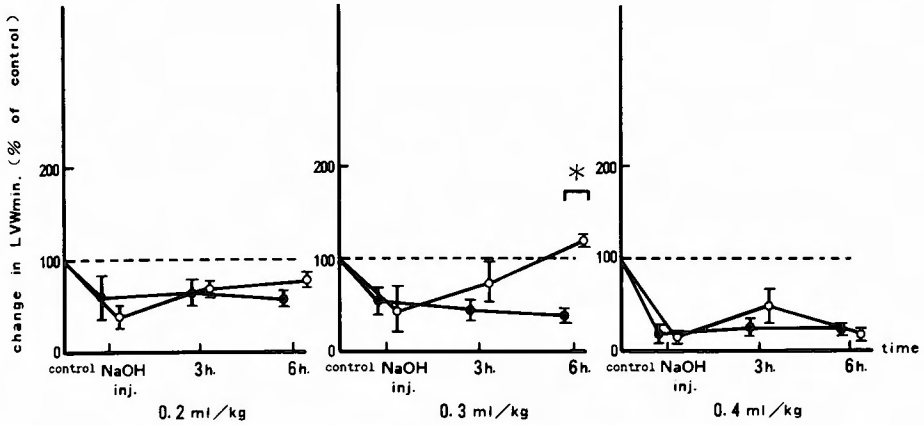


Fig. 19. Consecutive changes in LVWmin. after 5N-NaOH injection.

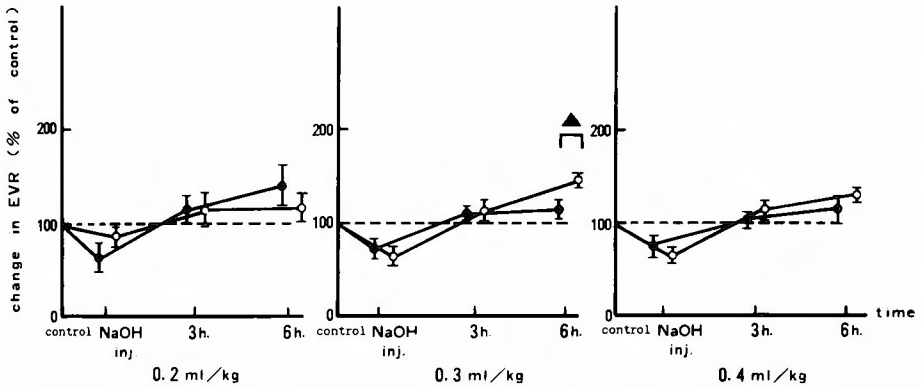


Fig. 20. Consecutive changes in EVR after 5N-NaOH injection.

resulted from the improved contraction force of the myocardium, because both preload and afterload were reduced by IABP.

The left ventricular work per minute, an index of the mechanical performance of the left ventricle, increased by IABP with cardiac output, and the difference between the IABP (+) and IABP (-) groups was significantly large in the 0.3 ml/kg group.

EVR, which indicates the supply-and-demand balance of oxygen in the myocardium, was enhanced by IABP, and the difference between the IABP (+) and IABP (-) groups was significantly large in the 0.3ml/kg group 6hr after producing necrosis. Little improvement of EVR, however, was seen in the performance of IABP in the 0.2 ml/kg group with a relatively small area of necrosis.

#### IV. Discussion

##### 1. Heart Failure Model

With the rapid progress of cardiac surgery, there has been considerable improvements in the operation results. One problem remains, however, as the cases become more critical and the patients are older: how to cope with patients exhibiting power failure such as peri-operative or

post-operative refractory heart failure and cardiogenic shock. A number of mechanical devices have been designed and clinically applied, but the evaluation of their application standards, effects, and limitations in their clinical and phased use has not been established. A major cause for the absence of consensus is the lack of an established standard model of quantitated acute heart failure.

Dogs are commonly used as experimental subjects because of their availability, size, and ease of handling. The coronary artery ligation procedures<sup>13</sup> have been widely adopted for inducing myocardial infarction. Rapid ligation, however, frequently evokes ventricular arrhythmia, often fails to cause heart failure and to produce transmural infarction because of the development of collateral channels; moreover, these changes in the hemodynamic state are only transient. Ligation, if not performed on the main coronary artery, is not likely to produce a quantitative model demonstrating cardiogenic shock or heart failure<sup>14,53</sup>. In addition, the producing of myocardial infarction by ligation takes considerable time. Cox<sup>7</sup> et al. reported that in dogs with myocardial infarction prepared by ligation, myocardial ischemia developed immediately after ligation with maximal ischemia being seen at about 18hr. Myocardial necrosis appeared 12hr after ischemia and reached a peak later than that of ischemia. The commonest technique for the producing a heart failure model is the multiple ligation method<sup>23,24,29,35,39,45,46</sup>, in which multiple ligations are performed on the left anterior descending artery (LAD) and the circumflex artery. There are, however, many problems with the method: 1) It is difficult to control the area of infarction. SHIOZAWA<sup>46</sup> et al., producing infarction in dogs, found that the area ranged from 20 to 60% of the free wall of the left ventricle by ligating LAD at the first diagonal branch, and all the branches from the right coronary artery and the left circumflex artery perfusing the LAD region. 2) The infarction is limited to a small area in the anterior wall of the left ventricle near the apex; producing infarction at an arbitrary site such as in a high portion of the lateral wall is difficult. 3) Production of transmural infarction is not ensured. 4) Fatal arrhythmia, such as ventricular fibrillation, frequently results in increased mortality. 5) Considerable time is required to produce necrosis. For these reasons, the multiple ligation method does not seem to be suitable for producing a quantitated model of heart failure.

In the present experiment, the direct injury method with 5N-NaOH described by MATSUMURA<sup>19</sup> et al. was adopted, and its merits as a procedure to minimize the influence on the entire body and to complement the weaknesses of the ligation methods were confirmed. Quantitation of heart failure was made possible using this method by determining the area of necrosis with different volumes of injection. An injection of 5N-NaOH (2ml) into the free wall of the left ventricle consistently produced a nearly circular edematous area, 1.5 to 2 cm in diameter, at the injection site, which developed in about 30 minutes into a necrotic area, 2 to 3 cm in diameter, with clear boundaries. In the horizontal sections fixed with a 10% formalin solution, areas of blackish, transmural necrosis, clearly differentiated from the surrounding myocardium, were observed. Pathohistological observations confirmed the uniformity of the histological features of the area, and the similarity of the necrotic and the surrounding degenerative areas to those of acute myocardial infarction ordinarily encountered clinically.

The strong positive correlation between the injection volume and the weight of the necrotic area demonstrates the adequacy of the method for producing an acute myocardial infarction model with quantitated areas of transmural infarction.

As for the changes in hemodynamic state, the severity of the heart failure increased with increase either in the 5N-NaOH injection volume or in the necrotic area. Six dogs in the 0.3 ml/kg and 8 in the 0.4 ml/kg injection groups die within 1 hr of producing the necrosis. Hemodynamic data on the 27 dogs within 30 min. of producing the necrosis shows deterioration of heart failure associated with the increase in the injection volume. Especially, cardiogenic shock was apparent in the 0.4 ml/kg group with mean sAoP of 70.6 mmHg, mean LVEDP 16.6 mmHg, CI 1.43/min./M<sup>2</sup>, and mLAP 15.9 mmHg. The marked decline in the cardiac output in this period presumably resulted from the decrease in the stroke volume due to the myocardial necrosis, which ranged from 35.5% to 46.0% of the left ventricle.

The size of the infarct area is the primary factor in determining the function of the left ventricle, or the occurrence of critical heart failure and cardiogenic shock<sup>37,43</sup>. SWAN<sup>48</sup> et al. investigating a hemodynamic model of myocardial infarction reported that the decrease in the stroke volume is determined by the range of infarction. PAGE<sup>37</sup> et al. reporting their clinical observations found that the ratio of the necrotic area was over 40% in the cases that died of cardiogenic shock. The reports cited above are in accordance with the results of the present study. FORRESTER<sup>13</sup> et al. classified hemodynamic states by the degree of reduction in CI and increase in pulmonary capillary wedge pressure (PCWP):

Subset I—CI > 2.2 l/min./M<sup>2</sup>, PCWP < 18 mmHg

Subset II—CI > 2.2 l/min./M<sup>2</sup>, PCWP > 18 mmHg

Subset III—CI < 2.2 l/min./M<sup>2</sup>, PCWP < 18 mmHg

Subset IV—CI < 2.2 l/min./M<sup>2</sup>, PCWP > 18 mmHg

Prognosis was best for Subset I and worst for Subset IV. Mortality was 3%, 9%, 23%, and 51% for the respective groups. The 0.2 ml/kg 5N-NaOH-injection group in the present experiment falls under Subset I or II, 0.3 ml/kg group under Subset III, and 0.4 ml/kg group under Subset IV. Mortality in the present experiment was 40% for the 0.3 ml/kg group and 47% for the 0.4 ml/kg group. The heart failure model of the present experiment was hemodynamically similar to FORRESTER's<sup>13</sup>

The method for producing a model of myocardial infarction reported by MATSUMURA et al. was adopted, since it was most suitable for the purpose of the present study; namely, to evaluate the effects and limitations of IABP using a model of left heart failure with irreversible, quantitated myocardial necrosis.

## 2. Effects and Limitations of IABP

Intra-aortic balloon pumping, devised by MOULOPOULUS<sup>31</sup> et al. and clinically applied first by KANTROWITZ<sup>21</sup> et al., has become a most widely used technique for assisting circulation in the clinical field, mainly due to the ease of its manipulation and its relatively negligible effects on hemolysis. Its mechanism is based on the effect of counterpulsation produced by deflating and

inflating the balloon at the systole and diastole respectively in the thoracic descending aorta, usually synchronized with the electrocardiographic responses. Inflation of the balloon at the diastole causes an elevation of the aortic diastolic pressure, or diastolic augmentation, and an increase in the coronary blood flow<sup>50,57)</sup>. With its deflation at the systole, on the other hand, the rapid contraction of the balloon volume reduces the aortic systolic pressure, which in turn reduces systolic impedance and decreases afterload by systolic unloading<sup>5,52,55)</sup>. The effect of IABP always consist of these two aspects.

In applying IABP in acute heart failure resulting from myocardial ischemia, a continuous performance of at least 2 to 3hr is reported to be necessary<sup>27,42)</sup>, there is of course some variance depending on the area and the degree of the ischemia, in order to restore the contraction force of the heart by increasing the coronary blood flow. A minimum of 6hrs of pumping is also known to be necessary to achieve sustained effects of IABP long after its cessation<sup>20)</sup>. The earlier reports were supported by the results of the present experiment; namely, significant changes appeared 3 to 6hr after producing the necrosis in such indices as HR, mAoP, CI, SVI, SWI, LVWmin., and EVR.

The mechanism of the effects of IABP is considered as follows:

The diastolic augmentation by IABP enhances the mean aortic pressure and increases blood perfusion through the coronary vessels<sup>50,51,57)</sup>. This elevates EVR, reflecting a better supply-and-demand balance of oxygen in the myocardium, and improves SLVP and LVmax  $dp/dt$ , indicating a recovery of the contractility of the ventricle. Systolic unloading due to IABP, as reported by URCHEL<sup>52)</sup> et al., produces a reduction in systolic impedance of the left ventricle, which is demonstrated by the reduction in LVEDP and TSR, and assists the performance of the ventricle ejecting blood into the aorta. The increase in the contraction force by diastolic augmentation and the reduction in systolic impedance of the left ventricle by systolic unloading synergistically operate to induce an elevation of the stroke volume index, which, along with the recovery in the heart rate, increases the cardiac index. Finally the left ventricular work improves with the increase of the cardiac index, and its mechanical performance is restored.

The present study revealed, however, a variance in the effect of IABP associated with the size of the necrotic area. No significant difference was found for each index between the IABP (+) and IABP (-) groups in the 0.2 ml/kg group with relatively small necrotic areas or in the 0.4 ml/kg group with large necrotic areas. This suggests that the effect of IABP is determined by the size of necrosis.

In order to observe the direct influence of IABP on the hemodynamic state, the relation between the weight ratio of the necrotic area in the left ventricle and mAoP was evaluated. The subjects were divided into three groups according to the weight ratio of necrosis (15-25%, 25-35%, and over 35%), and the mean aortic pressure for each group with and without IABP was calculated (Fig. 21). The changes in the mean aortic pressure are represented as percentages of the values 6hr after producing the necrosis to the immediate post-necrosis values. In the 25-35% necrosis group, they were  $129.3 \pm 15.2\%$  (mean  $\pm$  SD) for the IABP (+) and  $100 \pm 19.6\%$  for the IABP (-) groups, the difference between the IABP (+) and IABP (-) groups being

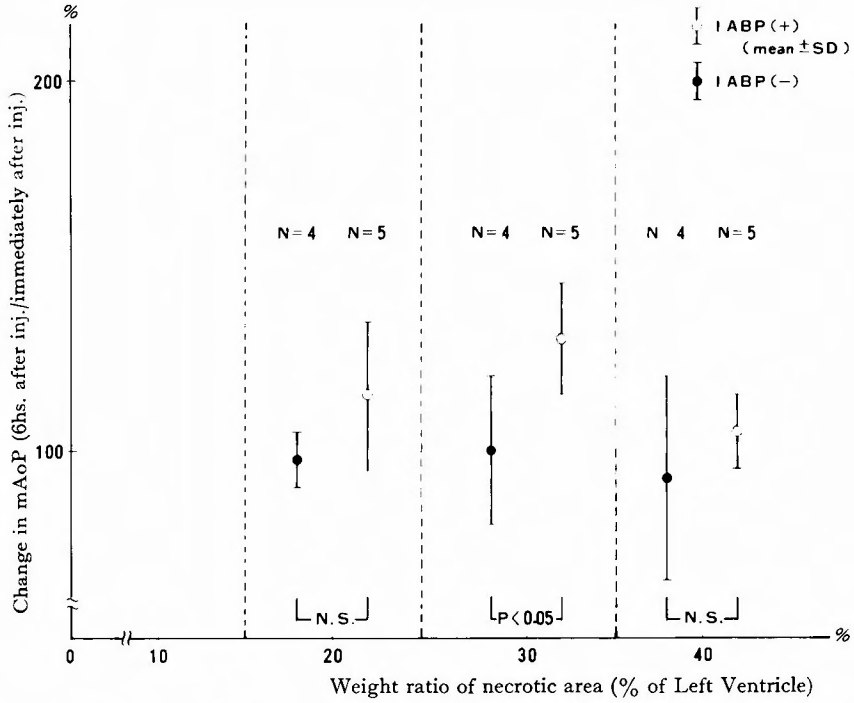


Fig. 21. Relation between changes in mAoP and weight ratio of necrotic area.

statistically significant ( $p < 0.05$ ). In the 15-25% and over 35% necrosis groups, however, the differences between the IABP (+) and IABP (-) groups were not significant (Table 5).

In order to examine the unloading of the left ventricular work by IABP, the efficiency of the left ventricular work was investigated. Among the many possible indices, the ratio of the work per minute to the unit oxygen consumption, or LVWmin. divided by TTI, was taken as its index (Fig. 22). TTI is known to be in directly proportional to the oxygen consumption<sup>41</sup>. The changes in LVWmin./TTI are represented, as in mAoP, as percentages of the values 6hr after producing necrosis to the immediate post-necrosis values. They were  $181.8 \pm 35.6\%$  for the

Table 5. Effect of IABP on mAoP and LVWmin./TTI.

Index \ Weight ratio of necrotic area (%)	15 ~ 25	25 ~ 35	35 ≤
	m A o P	97 ± 7.8 115 ± 19.0	100 ± 19.6 129 ± 15.2 △
L V W min. / TTI	75 ± 18.0 105 ± 14.4 △	82 ± 28.0 181 ± 35.6 ⊙	70 ± 23.0 96 ± 24.9

upper : IABP (-)  
lower : IABP (+)  
mean ± SD

none : NS  
△ : P < 0.05  
⊙ : P < 0.005

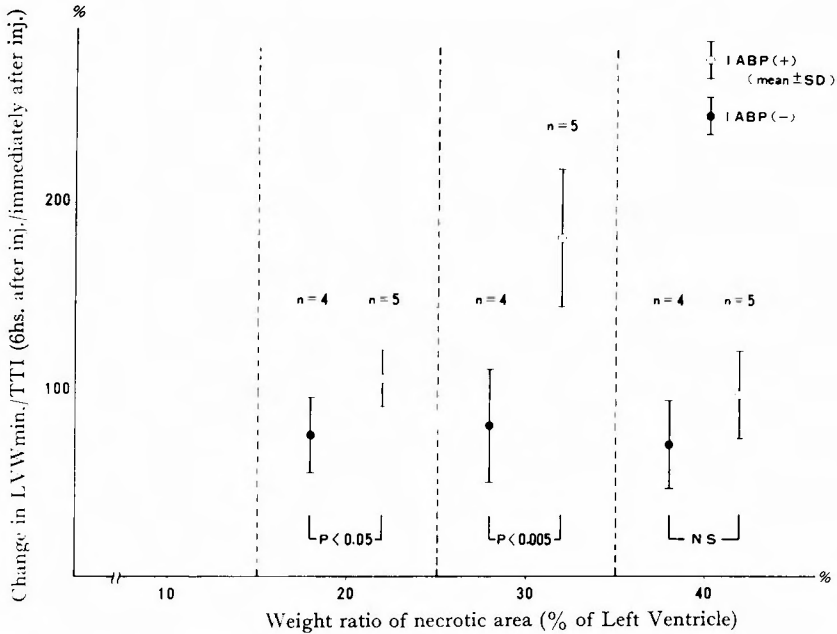


Fig. 22. Relation between changes in LVWmin./TTI and weight ratio of necrotic area.

IABP (+) and  $81.5 \pm 28.0\%$  for the IABP (-) groups in the 25-35% necrosis group; these differences were significant ( $p < 0.005$ ). In the over 35% necrosis group, however, no significant differences were found between the IABP (+) and IABP (-) groups (Table 5).

The above discussion on the two indices clearly suggests that IABP is most effective in cases with necrosis ratio between 25% and 35%, but less effective in milder heart failure with smaller necrosis ratio or in more serious cases with ratios over 35%.

The relation between the necrosis ratio and CI, the clinically most important index of cardiogenic shock<sup>13)</sup>, was also studied. The influence of preload may be excluded in discussing CI, since mLAP, which directly represents preload, was not significantly different between the IABP (+) and IABP (-) groups. Since the effect of IABP was found to be most notable for the cases with 25-35% necrosis in the earlier discussion on mAoP and LVWmin./TTI, the subjects were divided here into two groups with a necrosis ratio of 30% as the demarcation. The changes in CI are given as percentages of the values 6hr after producing the necrosis to the immediate post-necrosis values for each of the groups of different necrosis ratios with or without IABP application (Fig. 23). For the group with necrosis ratios less than 30% and treated by IABP, the linear regression equation,

$$y = 8.69x - 65.34 \quad (n=9, r=0.875, p < 0.05),$$

was obtained, and a strong positive correlation was confirmed. For the group with necrosis ratios over 30% and treated by IABP, a significant negative correlation was observed by the equation,

$$y = -6.56x + 363.8 \quad (n=6, r=-0.706, p < 0.05).$$

For the group showing 30% or more necrosis and not treated by IABP, the linear regression

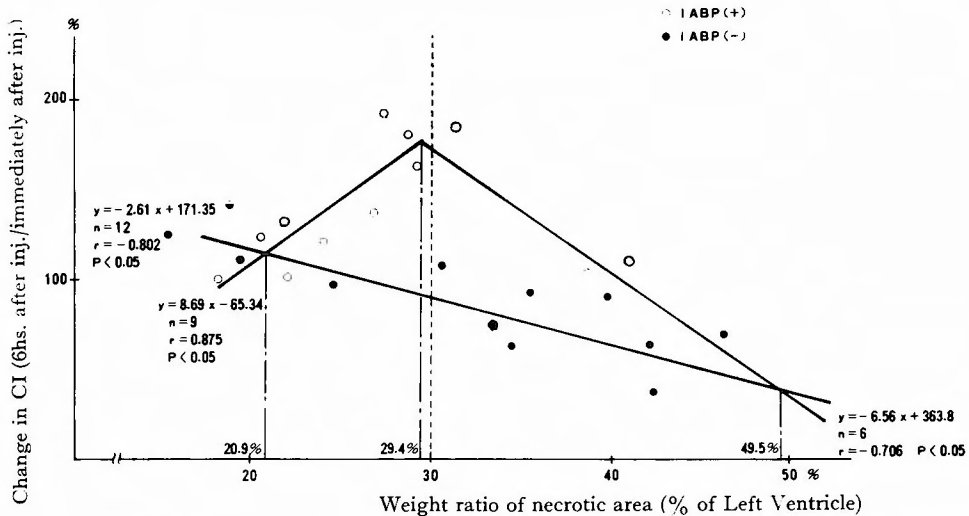


Fig. 23. Relation between changes in CI and weight ratio of necrotic area.

equation,

$$y = -2.61x + 171.35 \quad (n=12, r=-0.802, p<0.05),$$

was obtained, and a strong negative correlation was observed. When these three equations were set in the same coordinates, a triangle surrounded by the three lines was obtained, which represents the increment of CI brought about by the application of IABP. The necrosis ratio at the top of the triangle, or the point where the effect of IABP is maximum, was 29.4%. At the other two apexes of the triangle, where the increment of CI due to IABP becomes nil, the ratios of necrosis were 20.9% and 49.5%. The results indicate that the effect of IABP cannot be expected in the cases with either less than 20% or more than 50% necrosis ratios.

There has been no consensus as to the limitations of the effect of IABP in acute myocardial infarction. BOLOOKI<sup>3)</sup> reported that IABP failed to save patients with infarction of over 50% of the left ventricle, as confirmed by autopsy. MUNDTH<sup>33)</sup> et al. showed that the application of IABP alone was not adequate for the cases in which over 30% of asynergy was observed angiographically. INOUE<sup>20)</sup> suggested infarctions of 65% of the surface area of the left ventricular free wall as the limits for the effect of IABP. The absence of consensus among investigators seems to be derived from disparities in their experimental procedures, selection of subjects, and methods of measurement. In the present experiment, a model of acute left heart failure with a quantitated transmural necrosis was successfully produced. The myocardial necrosis in the model was pathogenically different from, but histologically similar to, that commonly encountered in the clinical field. Therefore, the evaluation of IABP using this accurately quantitated model should be of significance.

IABP presently is an established technique for assisting circulation with its notable effect and accompanying physiological influence, as shown in the present study. It has been clinically applied chiefly to cardiogenic shock due to acute myocardial infarction<sup>10,18,21,44)</sup> and to the low cardiac output syndrome after cardiac surgery<sup>1,14,38,49)</sup>. Further applications have been to

arrhythmia<sup>34)</sup> and impending infarction<sup>17)</sup> induced by severe myocardial ischemia to prevent and control the development of infarction<sup>25)</sup> because of its effectiveness in increasing the coronary blood flow and improving the efficiency of the ventricular work. There are, however, limitations to IABP in relation to the degree of heart failure, since it is essentially a pressure assisting device. The cases with no increase in CI, a clinically useful index, after 6hr of sustained IABP application are presumed to have a 50% or more necrosis ratio, and the effect of IABP alone is expected to be insufficient. A flow assist method should be introduced as early as possible.

## V. Conclusion

The effects and limitations of IABP were examined in the present study, using a model of quantitated acute left heart failure produced by the direct injury method.

The effects of IABP were demonstrated by the significant changes in such indices as HR, mAoP, SVI, CI, SWI, LVWmin., and EVR 3 to 6hr after its application. These effects were presumably produced by the following mechanism: First, the diastolic augmentation by IABP elevates the aortic diastolic pressure and increases coronary blood flow. This enhances EVR, an index reflecting the supply-and-demand balance in myocardium, and, as a result, improves cardiac function. Secondly, its systolic unloading effect reduces the ejection impedance and pumps out blood more easily from the left ventricle. The two aspects of IABP work synergistically to induce an increase in the stroke volume index and, consequently, in the cardiac index. The increase in CI results in the improvement of the left ventricular work per minute, and the mechanical performance of the left ventricle is finally restored. These effects of IABP were maximum when the weight ratio of the necrotic area was 30% of the left ventricle.

IABP, essentially a pressure assisting device, has its limitations; its effects cannot be expected when the necrosis ratio is over 50%. A more suitable flow assisting device should be applied in such cases.

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## References

- 1) Ban T, Nishiwaki N, et al: Coronary artery bypass grafting combined with intracardiac procedures. *Heart* **14**: 46-54, 1982. (in Japanese)
- 2) Berger RL, McCornick JR, et al: Successful use of a paracorporeal left ventricular assist device in man. *JAMA* **243**: 46-49, 1980.
- 3) Bolooki H: Clinical application of intra-aortic balloon pump. New York, Futura Publishing Inc 1977. p. 339.
- 4) Buckberg GD, Fixler DE: Experimental subendocardial ischemia in dogs with normal coronary arteries. *Cir Res* **30**: 67-81, 1972.



- 5) Chatterjee S, Rosenweig J: Evaluation of intraaortic balloon counterpulsation. *J Thorac Cardiovasc Surg* **61**: 405-410, 1971.
- 6) Connolly JE, Becaner MB, et al: Mechanical support of the circulation in acute heart failure. *Surgery* **44**: 255-262, 1958.
- 7) Cox JL, McLaughlin VW, et al: The ischemic zone surrounding acute myocardial infarction. Its morphology as detected by dehydrogenase staining. *Am Heart J* **76**: 650-659, 1968, p. 125.
- 8) DeBakey ME: Left ventricular bypass pump for cardiac assistance. *Am J Cardiol* **27**: 3-11, 1971.
- 9) Dubois EF: Basal metabolism in health and disease. Philadelphia, Lea and Febiger Inc 1936, p. 125.
- 10) Dunkman WB, Leinbach RC, et al: Clinical and hemodynamic results of intraaortic balloon pumping and surgery for cardiogenic shock. *Circulation* **46**: 465-477, 1972.
- 11) Ellis PR, Bailas NJ, et al: Experimental heart failure in dogs. *Arch Surg* **89**: 229-306, 1964.
- 12) Forrester JS, Diamond GA, et al: Correlative classification of clinical and hemodynamic function after acute myocardial infarction. *Am J Cardiol* **39**: 137-145, 1977.
- 13) Forrester JS, Diamond GA, et al: Medical therapy of acute myocardial infarction by application of hemodynamic subsets. *New Engl J Med* **295**: 1356-1362, 1976.
- 14) Fujiwara T, Takanashi Y, et al: Clinical results of the intraaortic balloon pumping after cardiac surgery. *Jap J Thorac Surg* **34**: 497-503, 1981. (in Japanese)
- 15) Geoffery Farrer-Brown: A colour atlas of cardiac pathology. London, Wolfe Medical Publications Ltd 1977, p. 76.
- 16) Gerein AN, Jones RD, et al: Cardiac bypass with the pumpoxygenator for circulatory support during cardiac decompensation. *Surg Forum* **11**: 216-218, 1960.
- 17) Gold HK, Leinbach RC, et al: Refractory angina pectoris: Follow-up after intraaortic balloon pumping and surgery. *Circulation* **54**: Suppl III 41-46, 1976.
- 18) Ida T: Clinical studies on the effects of intraaortic balloon pumping in cardiogenic shock due to acute myocardial infarction. *JJATS* **29**: 8-25, 1981. (in Japanese)
- 19) Ino T, Hizuki Y, et al: Experience of use of long time V-A bypass for severe circulatory failure post cardiac surgery. *Jap J Thorac Surg* **34**: 877-882, 1981. (in Japanese)
- 20) Inoue T, Kiso K: Intra-aortic balloon pumping. Physiological considerations and clinical application. *JJATS* **24**: 885-893, 1976. (in Japanese)
- 21) Kantrowitz A, Tjønneland S, et al: Initial clinical experience with intraaortic balloon pumping in cardiogenic shock. *JAMA* **203**: 135-140, 1968.
- 22) Kolobov T, Zapol WM, et al: Partial cardiopulmonary bypass lasting up to seven days in alert lambs with membrane lung blood oxygenation. *J Thorac Cardiovasc Surg* **60**: 781-788, 1970.
- 23) Lass J, Campbell CD, et al: Preservation of ischemic myocardium with TALVB using complete left ventricular decompression. *Trans Am Soc Artif Int Organs* **25**: 220-225, 1979.
- 24) LeGal YM, Martlett RB, et al: Mechanical circulatory support in experimental animals with acute myocardial infarction. *Trans Am Soc Artif Int Organs* **25**: 210-215, 1979.
- 25) Leinbach RC, Gold HK, et al: Early intraaortic balloon pumping for anterior myocardial infarction without shock. *Circulation* **58**: 204-210, 1978.
- 26) Liwak RS, Loffsky RM, et al: Use of a left heart assist device after intracardiac surgery: Technique and clinical experience. *Ann Thorac Surg* **21**: 191-202, 1976
- 27) Matsukura H: Assisted circulation. Hemodynamic and metabolic effects of intraaortic balloon pumping on acute ischemic left heart failure in dogs. *JJATS* **23**: 279-296, 1975. (in Japanese)
- 28) Matsumura M: Experimental study on quantitative left heart failure model and effect of trans-apical left ventricular bypass. *Medical J Hiroshima Univ.* **29**: 397-419, 1981. (in Japanese)
- 29) McDonnell MA, Karlios AC, et al: Comparative effect of counterpulsation and bypass on left ventricular myocardial oxygen consumption and dynamic before and after coronary occlusion. *Am Heart J* **97**: 78-88, 1979.
- 30) Miura I, Akimoto T, et al: Clinical review of 207 acute myocardial infarction. Results of treatment in CCU and a few discussions. *Heart* **2**: 1246-1264, 1970. (in Japanese)
- 31) Mouloupoulos SD, Topaz S, et al: Diastolic balloon pumping (with carbon dioxide) in the aorta—A mechanical assistance to the failing circulation. *Am Heart J* **63**: 669-675, 1962.
- 32) Mueller H, Ayres SM, et al: The effects of intra-aortic counterpulsation on cardiac performance and metabolism in shock associated with acute myocardial infarction. *J Clin Invest* **50**: 1885-1900, 1971.
- 33) Mundth ED: Mechanical and surgical interventions of the reduction of myocardial ischemia. *Circulation* **53**: Suppl I 176-183, 1976.

- 34) Murata S, Tatsuta N, et al: The method and the effect of manipulating IABP in cardiac arrhythmia. *JJATS* **29**: 678-680, 1981. (in Japanese)
- 35) Nakamura T: Experimental studies of the effect of intraaortic balloon pumping for asynergy due to acute myocardial infarction. *JJATS* **28**: 911-923, 1980. (in Japanese)
- 36) Okura M, Soma Y, et al: Clinical study of assisted circulation following cardiopulmonary bypass. Venous-arterial bypass combined with intra-aortic balloon pumping. *Jap J Thorac Surg* **34**: 871-876, 1981. (in Japanese)
- 37) Page DL, Caulfield JB, et al: Myocardial changes associated with cardiogenic shock. *New Engl J Med* **235**: 133-137, 1971.
- 38) Parker FB Jr, Neville JF, et al: Intraaortic balloon counterpulsation and cardiac surgery. *Ann Thorac Surg* **17**: 144-151, 1974.
- 39) Pennock JL, Pae WE Jr, et al: Reduction of myocardial infarct size: Comparison between left atrial and left ventricular bypass. *Circulation* **59**: 275-279, 1979.
- 40) Philips PA, Bregman D: Intraoperative application of intraaortic balloon counterpulsation determined by clinical monitoring of the endocardial viability ratio. *Ann Thorac Surg* **23**: 45-51, 1977.
- 41) Sarnoff SJ, Braunwald E, et al: Hemodynamic determinants of oxygen consumption of the heart with special references to the tension-time index. *Am J Physiol* **192**: 148-156, 1958.
- 42) Sedek GS, Zochowsky RJ, et al: Demonstration of lack of persistence of effectiveness of intra-aortic balloon pumping of short duration in acute myocardial ischemia. *Trans Am Soc Artif Intern Organs* **21**: 555-565, 1975.
- 43) Scheidt S, Ascheim R, et al: Shock after acute myocardial infarction: A clinical and hemodynamic profile. *Am J Cardiol* **25**: 556-564, 1970.
- 44) Scheidt S, Wilner G, et al: Intra-aortic balloon counterpulsation in cardiogenic shock. Report of a cooperative clinical trial. *New Engl J Med* **288**: 979-984, 1973.
- 45) Shigemori R: Experimental and clinical studies of IABP in ischemic heart. *JJATS* **27**: 1221-1234, 1979. (in Japanese)
- 46) Shiozawa T: Experimental and clinical studies on the effect of intraaortic balloon pumping for cardiogenic shock due to acute myocardial infarction. *JJATS* **26**: 1501-1517, 1978. (in Japanese)
- 47) Swan HJC, Forrester JS, et al: Hemodynamic spectrum of myocardial infarction and cardiogenic shock. A conceptual model. *Circulation* **45**: 1097-1110, 1972.
- 48) Swan HJC, Forrester JS, et al: Power failure in acute myocardial infarction. *Prog Cardiovasc Dis* **12**: 586-600, 1970.
- 49) Takano H, Kawashima Y, et al: The early hemodynamic response to intra-aortic balloon pumping in patients with severe left heart failure. *Artif Organs* **7**: 123-126, 1978. (in Japanese)
- 50) Talpins NL, Kripke DC, et al: Counterpulsation and intraaortic balloon pumping in cardiogenic shock: Circulatory dynamics. *Arch Surg* **97**: 991-997, 1968.
- 51) Tamura M, Takeuchi K, et al: Effects of intraaortic balloon pumping on left ventricular performance. *JJATS* **23**: 263-271, 1975. (in Japanese)
- 52) Urchel CW, Eber L, et al: Alteration of mechanical performance of the ventricle by intraaortic balloon counterpulsation. *Am J Cardiol* **25**: 546-551, 1970.
- 53) Vansant JH: Technique of experimental ligation of the anterior descending coronary artery. *Surgery* **49**: 387-391, 1961.
- 54) Webb WR: Intraaortic balloon pumping. *Ann Thorac Surg* **21**: 572-572, 1976.
- 55) Weber KT, Janicki JS: Coronary collateral flow and intraaortic balloon counterpulsation. *Trans Am Soc Artif Int Organs* **19**: 395-401, 1973.
- 56) Weil MH, Shubin H: Shock following acute myocardial infarction. Current Understanding of hemodynamic mechanisms. *Progr Cardiovasc Dis* **11**: 1-17, 1968.
- 57) Yahr WZ, Butner AN, et al: Cardiogenic shock: Dynamics of coronary blood flow with intraaortic phaseshift balloon pumping. *Surg Forum* **19**: 142-143, 1968.

## 和文抄録

定量的心不全モデルを用いた大動脈内バルーンポンピングの  
効果と限界についての実験的研究

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今日心臓外科の進歩はめざましく、その手術成績は一段と向上して来た。しかし手術例の高令化、重症化に伴ない、術中術後の心ポンプ失調による心原性ショック、重症心不全等に対してはもはや薬剤のみでは救命できないものが多く、何らかの補助循環装置が必要となる。

現在まで多くの補助循環法が考案され臨床応用されているものも多いが、臨床上段階的に補助循環装置を使用していく上で補助循環法の適応基準、効果、限界等の評価は未だ議論の多いところである。このように評価の定まらない最大の理由は研究方法、および対象が一定していないことにある。

そこで著者は直接心筋壊死法による定量化された急性左心不全モデルを用い、現在最も広く臨床応用されている補助循環装置である大動脈内バルーンポンピング（以下 IABP）をとりあげ、その効果を血行動態および心機能から評価するとともに、その限界についても考察を加え、より強力な補助循環装置を使用していくべき時期、適応についても言及した。

その結果

1) 雑種成犬46頭に対し 5N-NaOH 注入により、貫壁性で境界鮮明な心筋壊死部を作成することができ、

その病理組織像は日常遭遇する急性心筋梗塞と同様な変化を示した。また 5N-NaOH 注入量と作成された心筋壊死量とは良好な正の相関を示し、血行動態でも注入量の増加に伴ない心不全はより重篤となった。すなわち本実験で使用された急性左心不全モデルは定量化されたものであり、補助循環法の評価に最適のモデルであることが証明された。

2) 定量化された急性左心不全モデルに対して IABP を使用することにより血行動態および心機能の改善を認めた。すなわち IABP は冠血流量を増し、心筋酸素需給バランスを反映する EVR を上昇せしめ、心収縮能を改善するとともに、左室駆出抵抗を減弱せしめ、心拍出量を増大し左室の mechanical performance を増す。

3) 大動脈平均圧、仕事効率、および心係数の IABP 施行6時間後の各変化と心筋壊死量との関係から IABP の効果を検討すると、心筋壊死量約30%（対左室量比）で効果は最大であった。しかし心筋壊死量50%を越えるものについては、血行動態を維持するには pressure assist の補助循環装置である IABP では、もはや効果は期待できず、より強力な flow assist の補助循環装置が必要であることが示唆された。